

PROSPECTUS FOR THE
UNIVERSITY OF MINNESOTA
CANCER CENTER

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ABSTRACT

The following pages state the case for the establishment of a Cancer Center at the University of Minnesota. The University's Medical School proposes to create the center in cooperation with the Colleges of Biological Sciences, Pharmacy, and Veterinary Medicine, the Schools of Dentistry and Public Health, and the University of Minnesota Hospital and Clinic.

The Medical School has made the establishment of this interdisciplinary program one of its top priorities and it is well positioned to utilize such a center productively. A strong faculty base already exists, many important cancer research programs are in operation and have received widespread recognition. Creating such a Cancer Center will help to focus and coordinate these various efforts, bring fiscal economy and intellectual cooperation to the venture, and provide participants with the resources necessary to make even more significant progress in the battle against cancer. The cancer initiative includes more than 75 faculty members. The Medical School faculty has earned \$14 million in research grants from cancer agencies, including the National Cancer Institute and the American Cancer Society. The University is requesting \$150,000 per year from the Legislature to provide administrative costs for initiation of the Cancer Center. These costs cannot be obtained through any other mechanism.

TABLE OF CONTENTS

Introduction	1
Objectives of the Cancer Center	2
Why at Minnesota?	3
Organization of the Center	4
Cancer Research Programs at Minnesota	5
Cancer Immunology	5
Cancer Chemoprevention	6
Cancer Cytogenetics	6
Cancer Cell Biology	6
Cancer Virology	7
Cancer Pharmacology	7
Cancer Biochemistry	8
Drug Design and Delivery	8
Cancer Epidemiology and Prevention	8
College of Veterinary Medicine	9
School of Dentistry	9
Clinical Programs	9
Program Organization and Financial Plan	11
Distribution of Endowed Earnings and Program Gifts	12

INTRODUCTION

The complex nature of biological research on the causes and treatment of cancer requires the intensive interaction of faculty talents from many disciplines. Investigators frequently consult with their colleagues to share knowledge. Often these researchers use the capabilities and resources of several laboratories to accomplish individual and combined objectives.

Cancer research represents an excellent example of the need to develop and focus basic science strengths to address critical problems of human biology and disease. It is vital to marshal knowledge of fundamental biology to resolve issues of cause, prevention, diagnosis and treatment. The recognition of this reality has led to the idea of creating the University of Minnesota Cancer Center. The University's already widely acclaimed programs dealing with malignant diseases will be coordinated in order to accelerate progress and improve care of cancer patients.

The interactions of Cancer Center scientists will be maximized by the development of cooperative personal relationships in education and research as well as joint equipment and resource utilization. The Center will provide optimal conditions for identifying new program directions, resources and personnel needs. It will encourage cooperative efforts in developing proposals and will help to focus cancer fundraising efforts.

A Cancer Center will provide unique opportunities not currently available. It will facilitate the development of research objectives specifically aimed at cancer research and will enable the Medical School to focus more effectively on strengthening its faculty. It will also help bring together basic and clinical scientists from many disciplines, thus fostering research initiatives and developing and implementing research funding.

Further, it will provide opportunities for improvements in cancer-related education and clinical care programs. And it will establish organizations and programs which are obligatory prior to seeking formal status of cancer center designation by the National Cancer Institute of the National Institutes of Health.

WHY AT MINNESOTA?

More than 100 Medical School faculty and 50 faculty from other collegiate units are currently researching the causes of cancer. During the 1986-87 fiscal year, the faculty of the Medical School received \$11.7 million in cancer research grants. This included \$8.6 million from the National Cancer Institute, \$2.3 million from the National Institute of General Medical Sciences, \$700,000 from the American Cancer Society, and \$100,000 from other cancer related agencies.

Three major Medical School-based private funds also support cancer research. These are the Children's Cancer Research Fund (\$400,000 per year), the Masonic Fund, including a professorship (\$300,000 per year) and a facilities pledge (\$500,000), and the Leukemia Task Force (\$200,000 per year).

The University of Minnesota has been broadly involved in national cancer research protocols. This includes departments involved in multidisciplinary National Cancer Institute sponsored groups such as the Cancer and Leukemia Group, the Radiation Therapy Oncology Group, the Gynecologic Oncology Group, the Eastern Cooperative Oncology Group, and the Children's Cancer Study Group. The University is also developing a Urologic Oncology Group. In summary, the University of Minnesota has a very active, ongoing clinical research program. Enhancement of present programs and efforts to improve already strong programs by the addition of equipment, personnel, and space are essential to provide excellence and treatment in clinical cancer research for Minnesota and the nation.

The University of Minnesota is one of the nation's leading clinical cancer research institutions. Many notable research clinicians work at the institution and most departments have strong ongoing clinical research activities. These include: Medical Oncology, Radiation Oncology, Gynecologic Oncology, Surgical Oncology, Pediatric Oncology, Neurology, Dermatology, Orthopaedic Surgery and Otolaryngology. Under the direction of the Cancer Task Force, a program has been developed to enhance the care and treatment of the cancer patient and to strengthen clinical research.

ORGANIZATION OF THE CENTER

The Center will be led by a **Director** responsible for developing and implementing the programs of the Center. This will include recruiting members in conjunction with home departments and collegiate units, developing budget and research proposals and financial overview. In addition it will entail developing educational programs in conjunction with faculty education committees and financial planning with University-based programs.

A **Council of Deans and Directors** from the Medical School, the College of Biological Sciences, the College of Pharmacy, Public Health, Dentistry, Veterinary Medicine and the University of Minnesota Hospital and Clinic will be responsible for establishing program policies and objectives, monitoring accomplishments, and securing budget approval. The Dean of the Medical School will chair the Deans Council.

An **Internal Scientific Advisory Committee** consisting of research faculty will be responsible for advising the Director in formulating and implementing scientific objectives and scientific and financial overview of the Center. This committee will be responsible for advising the Director on recruitment and for responding to and coordinating research initiatives.

An **External Scientific Advisory Committee** consisting of national experts in basic and clinical cancer research will meet annually to review the program and accomplishments of the Center and to provide a report to the Director and Council of Deans.

A **Community Advisory Committee** consisting of representatives of constituent organizations historically involved with cancer programs of the University of Minnesota and community leaders will review the programs and accomplishments of the Center. It will advise the Director on community relations and will work with the Director on financial development.

CANCER RESEARCH PROGRAMS AT MINNESOTA

The research spans several aspects of basic and clinically applied research. The strengths of the University of Minnesota in recent years have been in the area of developing laboratory animal model approaches to cancer and bringing these approaches to the patient in new and innovative treatment strategies. The program areas to be discussed include cancer immunology, cancer cell biology, carcinogenesis, cancer virology, cancer genetics, and the clinical cancer program.

1. Cancer Immunology

Cancer immunology efforts at Minnesota represent an important effort in the use of immunologic methods for understanding the biology of cancer, as well as developing new and important therapeutic advances. Emphasis ranges from understanding the biology of malignant cells of the immune system using immunologic and molecular genetic approaches, to the use of specific immunologic therapies, including adoptive cellular immunotherapy/lymphokine therapy and antibody-toxin therapy/bone marrow transplantation. These efforts are important strengths at the University since they are both involved in identifying the process of neoplasia development as well as producing new approaches to the therapy of these neoplasms.

Dr. Fritz Bach heads many important investigations into the immunobiology of cancer and is well supported by research grants. **Drs. John Kersey, Phil McGlave and Norma Ramsay** are responsible for the clinical and experimental bone marrow transplant program. This program focuses largely on the treatment of cancer, primarily leukemias and lymphomas, and is one of the largest in the world. Experimental studies conducted by the program's staff are directed at better ways to enhance tumor cell killing using antibodies and immunotoxins in conjunction with bone marrow transplantation.

Dr. Tucker LeBien and his colleagues are conducting studies in experimental leukemia cell biology using leukemic cells as a prototype. They have been producing monoclonal antibodies against surface molecules of these leukemic cells, and more recently have used growth factors and molecular genetic techniques in evaluating these diseases. **Dr. Daniel Vallera** directs a program which is developing immunotoxins for cancer therapy. This approach links antibodies to potent poisons resulting in the generation of highly toxic molecules which are very specific for cancer cells, thus resulting in cellular destruction while preserving normal tissue. This has been an extremely productive effort. It has been used successfully within the bone marrow transplant program.

Several current needs exist within the cancer immunology program. One is the recruitment of a strong individual who is outstanding in the cellular

immunotherapy approach. This will further facilitate development of adaptive immunotherapy. Recruitment is currently underway for such an individual. Another high priority need is for additional strengths in the molecular immunology and molecular genetics of cancer. The rapidly developing field of molecular genetics is being incorporated into the laboratories of **Drs. Kersey, LeBien, Vallera and Bach**. However, this important technology will require several additional faculty at various times.

2. Cancer Chemoprevention

The University of Minnesota has many strengths in the fields of chemoprevention and dietary prevention of cancer. These should be more vigorously exploited. **Dr. Lee Wattenberg's** laboratory has made important contributions that have entailed identification of many inhibitors of carcinogenesis and have provided data on mechanisms of inhibition and range of inhibitory effects. **Dr. Wattenberg's** laboratory has a research program which is well funded by the NCI/NIH. **Drs. Danuta Malejka-Giganti and Helmut Gutmann** have done important work in carcinogenesis which provides a basis for chemopreventive strategies. **Dr. Richard Estenson** has a long history of studies relevant to tumor promotion which is an important aspect of carcinogenesis. **Dr. Bernard Mirkin** is pursuing investigations on preventing or controlling neuroblastomas. Other potential contributors include **Drs. Leo Furcht, Norman Sladek, and Patrick Hanna**. The strong cytogenetic and laboratory component of the Department of Laboratory Medicine and Pathology provides great potential strength for mounting a major effort in the diagnostic or predictive components of the work. As part of a cancer center, it will be possible to begin a major program in the fields of chemoprevention and dietary prevention of cancer.

3. Cancer Cytogenetics

Dr. Jorge Yunis currently heads a laboratory program focused on the cytogenic. The research is in several areas, including the molecular elucidation of fragile sites. A second area concerns the molecular understanding of multiple recurrent deletions and duplications often found in non-Hodgkin's lymphomas and solid tumors. A third area in **Dr. Yunis'** laboratory concerns cloning and characterization of a DNA sequence found in eighteen types of chromosomal rearrangements involved in different types of leukemias, preleukemia and lymphoma. Active cancer cytogenetic studies are underway in the laboratory of **Dr. Diane Arthur** in Laboratory Medicine and Pathology and **Dr. Clara Bloomfield** in Medical Oncology. These investigators are carrying out important studies of the chromosomal abnormalities in leukemia and lymphoma.

4. Cancer Cell Biology

The Medical School's Department of Laboratory Medicine and Pathology is extensively involved in cancer cell and molecular biology. This research seeks basic molecular answers to the causes and control of malignancy. Much of the expertise in cancer cell biology lies in two areas--blood and lymph cells, and metastatic cell biology and extracellular matrix.

Several important areas need to be developed. These include (1) oncogenes (hypothetic viral genetic material), both experimentally and in human tumors, (2) growth factors, (3) molecular dissection of metastatic cell behavior, (4) membrane receptors for cell matrix components, cell recognition molecules, and lymphoid cell surface molecules, (5) molecular studies on cell matrix components and the role they play in modulating tumor cell biology, (6) interplay of growth factors, matrix components, tumors and normal blood vessel development, and (7) gene rearrangments in malignancy.

5. Cancer Virology

The two major cancer virus groups presently being investigated at the University of Minnesota are: (1) retroviruses and (2) papillomaviruses. Within the retrovirus group most of the work is being done on Rous sarcomavirus and a member of the lentivirus subgroup, Visna virus. Two investigators are pursuing the mechanisms of replication and transformation by Rous sarcoma virus. **Dr. Perry Hackett** of the College of Biological Science's Department of Genetics and Cell Biology and the Institute of Human Genetics is studying the regulation of expression of retrovirus genes. **Dr. Anthony J. Faras** of the Department of Microbiology and the Institute of Human Genetics is investigating the mechanism of reverse transcription and the nature of endogenous retroviruses from avian as well as human sources. In the latter studies, Dr. Faras is collaborating with **Dr. Elwin Fraley** of the Department of Urologic Surgery to determine whether the C-type particles observed in cell lines obtained from germline tumors are related to new classes of human endogenous viruses and whether they play some role in oncogenesis. He is also studying the possible coordinated expression of certain oncogenes during papillomavirus infection.

Other oncogene work is currently being performed by **Dr. Janet Schottel** of the Department of Genetics and Cell Biology and **Dr. Clara Bloomfield** of the Department of Medical Oncology, **Dr. John Kersey** and **Dr. James Greenberg** of the Departments of Laboratory Medicine and Pathology and Pediatrics and the Institute of Human Genetics. The bulk of the lentivirus work ongoing at the University is being performed by **Dr. Ashley T. Haase** of the Department of Microbiology and is directed at central nervous system diseases. The papillomavirus work is currently being performed in the Institute of Human Genetics by **Dr. Faras** and **Dr. Ronald Ostrow**. Their work has two objectives. The first is to determine the mechanisms of transformation by papillomavirus. In those studies the cotton rabbit papillomavirus is analyzed as well as a model system with rabbits. The second study is directed at human disease and the involvement of human papillomavirus in chronic and recurring wart disease and malignant progression.

6. Cancer Pharmacology

Chemical carcinogenesis and the body dynamics of cancer chemotherapy comprise basic pharmacological research at the University's Medical School. **Dr. Norman Sladek** is active in this effort. An expanded program could take several directions. It is essential to encourage the development of a unique program built on existing strengths.

Emphasis must be placed upon the establishment of a powerful, fundamental, interdisciplinary research capability. A cohesive interdisciplinary program which incorporates pharmacology, biochemistry, immunology, molecular biology and genetics, the purpose of which is to study cellular growth and differentiation, would be ideal.

The transfer of new information generated by the basic research program to therapeutic application can in turn be facilitated and implemented by an active program in clinical pharmacology.

7. Cancer Biochemistry

A primary responsibility of the Department of Biochemistry is to serve as the focus of basic biochemical research in the Medical School. Cancer research employs these biochemical tools and requires a broad base of basic biochemical knowledge. Thus, all research in biochemistry is at least indirectly related to cancer and anything which builds the department's research strengths also strengthens its role in cancer research.

In specific relation to cancer research, a weakness of the department may be that, while several of its members work in biological areas related to the cause or treatment of cancer (e.g. gene regulation, nucleotide metabolism, protein toxins), no one of its members is primarily concerned with a problem directly related to cancer (i.e., could be called a cancer biologist). The department's contribution to cancer research would be strengthened by the addition of such a "cancer biologist" provided that this addition is complementary to existing and planned strengths. Current plans call for growth and development of the department secondarily in the area of molecular biology and primarily in the area of biophysics (spectroscopy, biomolecular structure, and dynamics).

8. Drug Design and Delivery

Improved methodologies for drug design and drug delivery systems show promise for providing significant advances in cancer therapy. Current studies include the synthesis of anti-viral and anti-cancer chemotherapeutic agents, molecular modeling, pharmacodynamics, and surface biochemistry. College of Pharmacy faculty who are leaders in this research include **Drs. Robert Vince, Terry Lybrand,**

Wayne Shier, Raj Suryanarayanan, Pat Hanna, Jadi Rahman, Yusuf Abul-Hajj, Cheryl Zimmerman and David Grant. Their research is linked with that of several other cancer researchers and their effectiveness would be enhanced by further integration of their work with other cancer researchers.

9. Cancer Epidemiology and Prevention

Epidemiology studies of cancer have yielded important information on the causes of cancer. In addition, there are known factors which influence the development of cancer to which education needs to be directed in order to change individual and community behavior. Faculty in the Schools of Public Health and Medicine who are involved in these and related areas include **Drs. Jack Mandel, John Potter Les Robison, Tom Louis and Henry Blackburn**. The current programs in cancer epidemiology and prevention emphasize childhood leukemia and colon cancer.

Dr. Richard King is the Director of a Familial Cancer Study Group (FCSG) that was established to develop a research and clinical program that will increase the knowledge of the genetic mechanisms of cancer and provide methods for risk assessment and prevention of cancer. This will be accomplished with an integrated, interdepartmental program that draws on existing strengths in oncology, genetics, epidemiology and molecular biology, and develop new areas of expertise for necessary components of the program. The five types of cancer being considered by the FCSG as possible candidates for a risk assessment and prevention program are colon, breast, testis, pancreas, and non-Hodgkins lymphoma.

10. College of Veterinary Medicine

Investigators at the College of Veterinary Medicine have made significant contributions to oncology research. Because the biologic behavior of many animal tumors is similar to those in man, animals with spontaneously occurring tumors provide an invaluable resource for studying basic cancer biology and evaluating innovative diagnostic and therapeutic procedures. The Cancer Center will strengthen existing basic research and clinical oncology programs, at the College of Veterinary Medicine by maximizing interactions between medical and veterinary investigators and enhancing cooperative efforts. More than a dozen faculty of the college, represented by veterinary oncologist **Dr. Jeff Klausner**, have expressed interest in the Cancer Center.

11. School of Dentistry

The School of Dentistry has conducted extensive research on various characteristics of oral, head and neck cancers. Specialized dental services are frequently required for patients receiving surgical, radiologic, chemotherapeutic or biotherapeutic treatment. Many departments within the

School of Dentistry contribute these services. Such commitment of faculty and space will broaden significantly under the impetus of a Cancer Center.

12. Clinical Programs

The University of Minnesota is internationally renowned for its contributions to clinical cancer research. As life expectancy continues to increase and as the baby boom population ages, cancer demographics will change dramatically. In twenty years, the number of individuals requiring clinical cancer treatment may well reach catastrophic proportions. A Cancer Center will position the University, with its historic strengths in clinical cancer programs, to deal with this situation.

Currently, **Drs. B.J. Kennedy and Clara Bloomfield** direct clinical research programs in medical Oncology. **Drs. Mark Nesbit, William Krivit and Norma Ramsay** guide the pediatric oncology program. Radiation oncology and therapeutic radiology clinical studies are conducted by **Drs. Seymour Levitt, Tai Kim** and others. Clinical research programs in gynecologic oncology are under the direction of **Drs. Leo Twiggs and Leon Adcock.**

Dr. George Adams conducts clinical research on head and neck cancers and **Drs. Robert Maxwell and Stephen Haines** direct clinical work in the area of neurologic tumors. Urologic cancer is being studied by **Drs. Elwin Fraley and Paul Lange.** **Dr. Louis Dehner** of the Department of Laboratory Medicine and Pathology leads an interdisciplinary clinical cancer conference.

PROGRAM ORGANIZATION AND FINANCIAL PLAN

The University of Minnesota Cancer Center will be a major interdisciplinary endeavor consisting of coordinated research and treatment programs. Senior scientists, working with more junior faculty and graduate students, will lead investigative teams which will focus on immunology, cell biology, carcinogenesis, virology, genetics, and the clinical cancer program. The program will be implemented over a five-year period.

Specific program costs are as follows:

1. **Endowed Professorships, \$9.0 million** -- Three positions would be funded by the interest from a \$9.0 million endowment. Endowments at the University yield 5.5% of the principal (\$495,000 in this case) with the remaining yearly interest returning to the principal to assure the perpetuity of the endowment.
2. **Junior Faculty Endowment, \$5.0 million** -- Five junior faculty positions would be established for the endowed professor. Funds for these positions would be established for a specified period to be applied to young scientists during the early stages of their careers. Junior faculty filling these positions would perform research within the programs and in support of the endowed professors.
3. **New Research Program Initiation (including laboratory equipment) -- \$2.5 million.** Within the broadly defined fields of oncology, neurology, otolaryngology, dermatology and orthopaedics, major research initiatives will emerge under the leadership of interdisciplinary, investigative teams.
4. **Facilities, \$13.5 million** -- A new 70,000 square foot facility would be constructed to house the Center. The building would contain research laboratories equipped with state-of-the-art technology as well as office and seminar space.

Total costs for the program -- \$30.0 million.

CANCER CENTER

	INITIAL GIFTS	YEAR 1		YEAR 2		YEAR 3		YEAR 4		YEAR 5	
		INCOME (SPENDABLE)	GIFT								
\$ 9 MILLION											
Endowed Professorships (3)											
Annual distribution @ 5.5%		165,000		254,925		348,897		447,097		549,716	
Endowment	3,000,000		1,500,000		1,500,000		1,500,000		1,500,000		
Cumulative endowment			4,635,000		6,343,575		8,129,036		9,994,842		10,444,610
\$ 5 MILLION											
Endowed Junior Faculty (5)											
Annual distribution @ 5.5%		55,000		112,475		172,536		235,301		300,889	
Endowment	1,000,000		1,000,000		1,000,000		1,000,000		1,000,000		
Cumulative endowment			2,045,000		3,137,025		4,278,191		5,470,710		5,716,892
\$ 1 MILLION											
Program Development			500,000		125,000		125,000		125,000		125,000
\$15 MILLION											
Start-up Costs:											
Equipment Costs	500,000		250,000		250,000		250,000		250,000		
Construction Costs	2,250,000		2,250,000		2,250,000		2,250,000		2,250,000		2,250,000
Total income		220,000		367,400		521,433		682,397		850,605	
Total gifts	6,750,000		5,500,000		5,125,000		5,125,000		5,125,000		2,375,000
Cumulative gifts	6,750,000		12,250,000		17,375,000		22,500,000		27,625,000		30,000,000
\$30 MILLION											
=====											